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## Special Article

# A Proposal for the Retrospective Identification and Categorization of Older People With Functional Impairments in Scientific Studies—Recommendations of the Medication and Quality of Life in Frail Older Persons (MedQoL) Research Group

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## A B S T R A C T

## Keywords:

Functional status  
frailty  
concept paper  
evidence-based medicine  
assessment

When treating older adults, a main factor to consider is physical frailty. Because specific assessments in clinical trials are frequently lacking, critical appraisal of treatment evidence with respect to functional status is challenging. Our aim was to identify and categorize assessments for functional status given in clinical trials in older adults to allow for a retrospective characterization and indirect comparison of treatment evidence from these cohorts. We conducted 4 separate systematic reviews of randomized and nonrandomized controlled clinical trials in older people with hypertension, diabetes, depression, and dementia. All assessments identified that reflected functional status were analyzed. Assessments were categorized across 4 different functional status levels. These levels span from functionally not impaired, slightly impaired, significantly impaired, to severely impaired/disabled. If available from the literature, cut-offs for these 4 functioning levels were extracted. If not, or if the existing cut-offs did not match the predefined functional levels, cut-off points were defined by an expert group composed of geriatricians, pharmacists, pharmacologists, neurologists, psychiatrists, and epidemiologists using a patient-centered approach. We identified 51 instruments that included measures of functional status. Although some of the assessments had clearly defined cut-offs across our predefined categories, many others did not. In most cases, no cut-offs existed for slightly impaired or severely impaired older adults. Missing cut-offs or values to adjust were determined by the expert group and are presented as described. The functional status assessments that were identified and operationalized across 4 functional levels could now be used for a retrospective characterization of functional status in randomized controlled trials and observational

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This project has been funded by the Baden-Wuerttemberg Ministry of Science, Research and Arts.

The authors declare no conflicts of interest.

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<https://doi.org/10.1016/j.jamda.2018.11.008>

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studies. Allocated categories only serve as approximations and should be validated head-to-head in future studies. Moreover, as general standard, upcoming studies involving older adults should include and explicitly report functional impairment as a baseline characteristic of all participants enrolled.

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To optimally tailor drug therapy in older adults to their specific needs, it is desirable to identify, evaluate, and critically appraise the available evidence with respect to not only chronological age but other factors. Epidemiologic longitudinal studies have demonstrated that functional status, disability, or frailty were more predictive for mortality or other relevant endpoints than, for example, the number of comorbidities or age alone.<sup>1–4</sup> As a consequence, at least some guideline committees are already working on separate recommendations for functionally impaired older adults.<sup>5</sup> However, evidence is still very limited because of the exclusion of functionally dependent patients from clinical studies and because it is impossible to compare cohorts in treatment studies with respect to functional status.<sup>6,7</sup>

Although the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) has recommended to include frail older adults in clinical trials in 1993,<sup>8</sup> most studies have not yet followed this advice. A few studies, however, did include frail older people. Recent examples are the Systolic blood Pressure Intervention Trial (SPRINT) and the Hypertension in the Very Elderly Trial (HYVET) for the treatment of arterial hypertension. Both have demonstrated positive effects of tighter blood pressure control, even in prefrail and apparently frail older adults, identified by the frailty index.<sup>9,10</sup> This does not resemble findings from observational studies that show that the more severely impaired may not benefit anymore.<sup>3,4</sup> These uncertainties often spark great controversies as observed with the development of the Joint National Committee (JNC-8) guideline on arterial hypertension.<sup>11–13</sup> The call for inclusion of frail people has been repeated in the 2007 statement paper by the European Medicines Agency (EMA),<sup>14</sup> such as the statement on points to consider on frailty (EMA/CHMP/778709/2015<sup>15</sup>) or the EU DIRECTIVE 2001/83/EC.<sup>16</sup> Frailty, however, is an extremely heterogeneous term, still awaiting an international consensus definition. It is accepted that frailty can be considered a vulnerable state that often results in disability, loss of autonomy, and dependency. Frailty is, therefore, subsequently tightly linked to functional status.<sup>17</sup>

Functional status can be characterized by measures of activities of daily living, performance-based tests on physical functioning, or interview-based questionnaires on functional abilities.<sup>18</sup> Functional

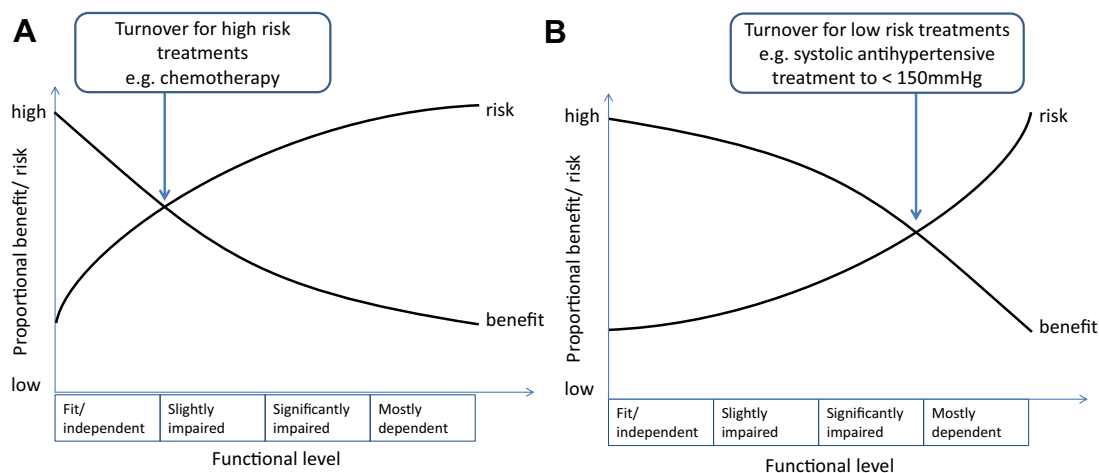
parameters can also be found in all tools on physical frailty and a variety of assessments addressing functional status have been developed and included in studies.<sup>19</sup> In addition to the International Classification of Diseases (ICD), the WHO has developed the International Classification of Functioning, Disability and Health (ICF) to standardize the assessment of health and disability across all social and cultural contexts.<sup>20</sup> Impaired functional status may result in dependency and disability, in line with the disablement process model by Verbrugge and Jette<sup>21</sup> and the ICF framework.

Nobody would ever question that functional status at least implicitly influences everyday treatment decisions in older people. As an example, high-risk treatments such as chemotherapy would in most cases not be considered appropriate for functionally impaired older people (Figure 1A). Our hypothesis is that for less aggressive treatments, the benefit-harm turnover, where the risk for harm is greater than the expected benefit, shifts toward the functionally severely impaired and disabled older people, but that it still does exist and has to be considered for most treatment decisions (Figure 1B). Therefore, all information on functional status that can be found in available clinical trials and observational studies should be used to classify treatment evidence across the functional trajectory.

For that purpose, all assessments that include a sufficient number of parameters on functional status could be used as proxies to approximately characterize the population of interest according to their functional level. This also applies to assessments on physical frailty. In the following, we will explain our rationale and why we are confident that this approach would be of use for the scientific community—at least until all new treatment studies include appropriate tests on functional status as well as a significant number of older adults with functional impairments.

## Methods

The Medication and Quality of Life research group is a German network by the Ruprecht-Karls University of Heidelberg, the Albrecht-Ludwigs University of Freiburg i. Br., and Ulm Universit. It consists of



**Fig. 1.** (A) Benefit-risk relation for treatment regimens that carry *high* risk for vulnerable older people. (B) Benefit-risk relation for treatment regimens that carry *low* risk for vulnerable older people.

geriatricians, internists, epidemiologists, neurologists, psychiatrists, clinical pharmacologists, and clinical pharmacists. The overall goal of the project is to identify the highest level of evidence for drug treatment of older people across different functional status levels and include this evidence in computer-adapted decision tools, taking into account individual preferences in order to facilitate treatment decisions in everyday clinical life. The first 2 work packages are devoted to the compilation of systematic literature reviews on common chronic diseases for older adults, beginning with arterial hypertension,<sup>22</sup> and the categorization of this evidence across different functional status levels. As part of 3 ongoing systematic reviews of randomized and nonrandomized controlled clinical trials in older people with hypertension, dementia, and diabetes, all assessments reflecting functional status identified in such trials were collected.

### Definition of Functional Categories

In order to rate the evidence across defined functional levels, the group first had to agree on the optimal and minimal number of categories needed to differentiate between treatments across different disease entities. A consensus was reached on categorizing functional status across the following 4 different levels to optimally account for findings from different clinical trials involving older adults and to account for clinical feasibility: (1) functionally independent,

(2) slightly impaired, (3) significantly impaired, and (4) severely impaired/disabled/dependent older adults. Figure 2 describes the prototypic person for each category. The category on the disabled, functionally severely impaired older adults includes all of those that are mostly or totally dependent on help by relatives or professionals, and often live in long-term care or nursing homes. Many assessments, especially those on frailty, lack information about this last (disability/dependency) category, which we consider necessary in order to discuss treatment recommendations for several slowly progressing chronic diseases.

### Identification of Functional and Physical Frailty Assessments

As part of 3 systematic literature reviews within a larger project on available evidence for drug treatment of frail older adults,<sup>22</sup> we identified assessments of physical function or physical frailty that were used in any of these studies. In addition, we conducted a nonsystematic search using the search terms *function(al) assessment*, *function(al) measure*, *function(al) test*, *frailty assessment*, *frailty score*, and *frailty scale* to identify additional indices, scores, and functionality/frailty measures that are related to functionality/frailty or, at least to some extent, relate to functional decline and/or disability. Our expert group added further instruments that were not found by the mentioned procedures. No additional restrictions were made.





	Independent	Person without relevant impairments, with unrestricted mobility, no problems to perform self care and usual activities
	Slightly impaired	Person with slight problems in walking, slight problems to perform all activities of daily living including instrumental activities, but still able to deal with them autonomously
	Significantly impaired	Person with significant problems in walking and coping with everyday issues, needing help by an assisting person in several activities of daily living, partially dependent on other persons
	Severely impaired/ disabled/mostly or totally dependent	Person with severe problems or unable to cope with everyday life actions, strongly restricted mobility or immobility, mostly or totally dependent, needing help by one or more assisting persons in most activities of daily living

Fig. 2. Proposed functional status levels for the retrospective characterization of study populations.

### Categorization of Assessment Quality With Respect to Functional Status

Following our concept, all applicable assessments had to report on physical functioning/functional status, and function measures should contribute substantially to the overall assessment or be reported separately. Ideally, most measures or questionnaires should be related to lower extremity and mobility domains because of their greater impact on activities of daily living and dependency.<sup>23</sup> All tools complying with these requirements were rated as functional quality category A. Assessments that contained rather few functional or physical frailty items or which only implicitly addressed these items (eg, within a rating of general health such as ASA, Karnofsky, or ECOG Performance Scores) were rated as category B. All assessments that solely addressed different concepts such as physical activity or morbidity or that did not allow differentiation of 4 functional levels according to our method were excluded.

After identifying the instruments, we proceeded to extract their cut-offs for the 4 defined functional levels. For those instruments where no cut-off values were established from the literature that resembled our predefined categories, or where the existing cut-offs did not match our functional concept, cut-offs based on functional status were proposed following these steps:

1. Critical evaluation of items, taking into account the maximum and minimum item results and item weights, the used scoring system and its clinical interpretation, followed by determining what *best* possible result a person could optimally obtain in a given functionality category in each item.
2. Determination of the upper cut-off points by counting the results, whereas the lower cut-offs result from the upper ones of the next lower functional status level.
3. Discussion and review of the results within the expert group and final statement.

With the resulting proposal, studies for diverse treatments in older people could be reevaluated according to functional status

of participants in order to construct Geriatric evidence maps. These maps should be clearly separated for functional status and for evidence levels according to standard approaches. They would list the number of studies showing a positive effect, neither a positive nor a negative effect, or a negative effect of a certain treatment for clinically relevant outcomes depending on functional status.

### Results

A total of 67,037 studies were screened as part of the 3 systematic reviews as described above. Complemented by the result of the non-systematic literature search and the additions of the expert group, 80 assessments were identified and critically evaluated. Twenty-nine assessments were excluded, and 51 were rated according to our predefined method. Forty-seven were assigned to category A and 4 to category B (Figure 3).

Possible cut-off points for this nonconclusive list of 51 instruments are presented in Tables 1 and 2. For better overview, frailty-oriented assessments are presented separately in Table 1, whereas Table 2 summarizes all other assessments that include functional status items and could be classified across our predefined functional categories. A list of included and excluded assessments with comments on the reasons for inclusion or exclusion can be found in Supplement 1. Ratings of individual assessment items are provided in Supplement 2.

Available cut-offs for all 4 defined functional levels were considered present in 5 of 51 assessments; 6 assessments had only predefined cut-offs for some of the functional levels (eg, without discrimination between “functionally independent” and “functionally slightly impaired”) and it was not possible to calculate the missing cut-offs. The remaining assessments were partly ( $n = 3$ ) or completely ( $n = 33$ ) processed according to our algorithm. For the clinical judgment scores ( $n = 4$ ), we had to estimate which clinical conditions mostly fit the 4 functional levels.

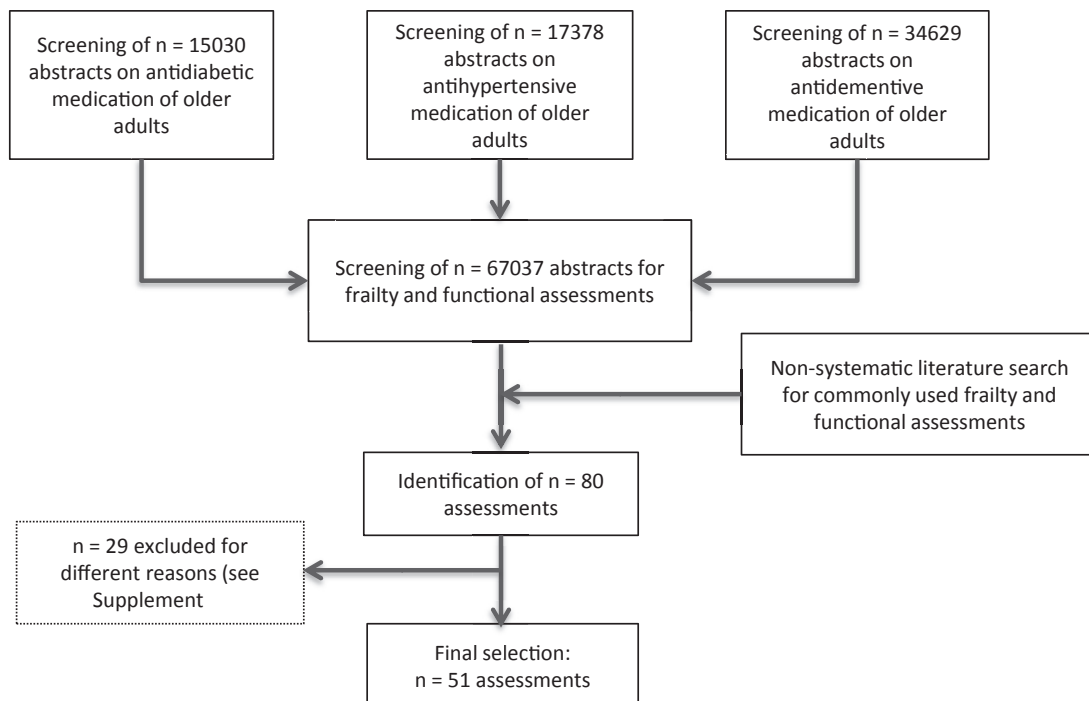


Fig. 3. Flow chart of the identification process of included assessments.

**Table 1**  
Frailty Indices and Scores to Categorize Patients According to Their Functional Status/Frailty Stage\*

Scores and Indices/ Functional Category	Functionally Independent	Functionally Slightly Impaired	Functionally Significantly Impaired/Partially Dependent	Functionally Severely Impaired/ Disabled/Mostly or Totally Dependent	Functional Quality Category
Comprehensive Assessment of Frailty (CAF) <sup>43,44</sup>	1-5	6-22	23-30	31-35	A
Cardiovascular Health Study (CHS, Fried) Frailty Scale <sup>17</sup>	0	0-2	3	4-5	A
Clinical Frailty Scale <sup>45</sup>	1-2	3-4	5-6	7-8	A
Frailty predicts death One year after Elective Cardiac Surgery Test (FORECAST) <sup>43,46</sup>	1	2-6	7-12	13-14	A
Gill Frailty Measure <sup>47</sup>	≤10 s to walk 3.0 m forth and back as quickly as possible and able to stand up from a chair with arms folded		>10 s to walk 3.0 m forth and back as quickly as possible or unable to stand up from a chair with arms folded	>10 s to walk 3.0 m forth and back as quickly as possible and unable to stand up from a chair with arms folded	A
Program of Research on Integration of Services for the Maintenance of Autonomy (PRISMA)—7 <sup>48</sup>	0	1-2	3	4-7	A
Frail Non-Disabled (FiND) Questionnaire <sup>49,50</sup>	0	0-1 (A/B)	2 (A/B) + 0-1 (C/D/E) = 2-3	2 (A/B) + 2-3 (C/D/E) = 4-5	A
Fatigue, Resistance, Ambulation, Illnesses, Loss of Weight (FRAIL) Scale <sup>51</sup>	0	0-1	2	3-5	A
Frailty/Vigor Assessment <sup>52</sup>	<4 frailty criteria, 4 vigor criteria		4 frailty criteria, ≤3 vigor criteria	>4 frailty criteria, ≤3 vigor criteria	A
FRail Elderly Support research group (FRESH) Screening Instrument <sup>53</sup>	0	0-2	3	4-5	A
Gérontopôle Frailty Screening Tool <sup>54</sup>	0	1	≥2		A
Groningen Frailty Indicator <sup>55</sup>	0	0-1	2-4	5-15	A
MacArthur Study of Successful Aging (MSSA) <sup>56</sup>	0	0-3	4	≥5	A
Study of Osteoporotic Fractures (SOF) <sup>57</sup>	0		1	2-3	A
Tilburg Frailty Indicator (Part B) <sup>58</sup>	0	1-4	5	6-15	A
Canadian Study on Health and Aging (CSHA, Rockwood) Frailty Index (min. 30 items) <sup>41</sup>	0-0.1	>0.1 and ≤ 0.21	>0.21 and ≤ 0.45	>0.45	A-B†

\*For the determination of cut-offs: see [supplement 2](#) and methods above.

†Depends on the index used in the study that is to be examined because index is composed individually in every study. Index should, therefore, be scrutinized with respect to items reflecting functional status.

## Discussion

We identified and categorized 51 assessments across 4 predefined functional status levels, which could now be used to characterize a study population according to functional status. We also defined categories that allow for quality ratings of all functional assessments identified. With our proposed approach, evidence maps for certain treatments in older people could be constructed, clearly separated for functional status and for evidence levels according to standard approaches.

To our knowledge, such an approach has not been taken before. We believe that our results can be useful for improving the critical appraisal of the available literature by setting the results of clinical trials into a functional perspective. This would improve information for stakeholders and health professionals on the (lack of) evidence on medical treatments across a trajectory of functionally independent older adults versus those with functional impairments up to disability and functional dependency.

Following our hypothesis, the benefit-risk relation of certain treatments changes along the trajectories of functional status depending on the clinical condition. Implications of this observation can be exemplified by different guidelines on arterial hypertension that recommend different systolic blood pressure targets for older people. Although most of them still endorse 150 mmHg for those >80 years old, newer trials such as the SPRINT study shatter these recommendations—even in frail older people. Frailty in SPRINT was measured by a modified frailty index as proposed by Rockwood.<sup>24</sup> This

frailty index was generated out of 37 items, of which only 4 items were related to functional status (gait speed, washing and dressing combined, limitations with moderate activities, and climbing a flight of stairs), applying a multidimensional approach to increasing vulnerability. According to our functional approach, it would be rated category B and should be critically appraised in evidence maps focusing on functional status. Therefore, SPRINT (or HYVET<sup>9</sup>) might not contradict findings from observational trials that included participants with higher functional impairments or disability such as the PARTAGE study in nursing homes<sup>3</sup> or a population-based study using data from the National Health and Nutrition Examination Survey.<sup>4</sup> Some guidelines have taken up these findings. For example, the 2013 ESH/ESC guideline recommends that in frail older adults blood pressure should be lowered as tolerated.<sup>25</sup> These results seem to be comparable to other chronic diseases such as chronic obstructive pulmonary disease<sup>26</sup> or osteoporosis,<sup>27</sup> where standard treatments could be recommended up to frail, but possibly not functionally severely impaired, activities of daily living—dependent older people. When treatments are known to possibly cause more severe adverse drug reactions, deviations from standard recommendations in older people could even become necessary earlier during the functional trajectory. Examples can be found for antidepressant medication of major depressive disorders,<sup>28</sup> or even more pronounced for chemotherapy<sup>29</sup> and treatment of diabetes with an increased risk of hypoglycaemia.<sup>30</sup>

Frailty instruments were also included and rated according to our approach. Although many focus on physical frailty and, therefore, include many functional status measures, many others do not. The



**Table 2**

Other Indices and Scores to Categorize Patients According to Their Functional Status\*

Scores and Indices/Functional Category	Functionally Independent	Functionally Slightly Impaired	Functionally Significantly Impaired/Partially Dependent	Functionally Severely Impaired/Disabled/ Mostly or Totally Dependent	Functional Quality Category
Barthel ADL-Index <sup>59</sup>	100	75-100	45-70	0-40	A
Berg Balance Scale <sup>60</sup>	55-56	38-54	9-37	≤8	A
Bristol ADL Scale <sup>61</sup>	0	1-7	8-36	≥37	A
Functional Independence Measure (FIM) <sup>62</sup>	126	105-126	64-104	18-63	A
5-Chair-Rise <sup>63</sup>	≤15 s		>15 s	Unable	A
Gait Speed <sup>64,65</sup>	≥1.0 m/s	<1.0 and ≥ 0.8 m/s	<0.8 and ≥ 0.5 m/s	<0.5 m/s	A
Groningen Activity Restriction Scale (GARS) <sup>66</sup>	18-21	22-36	37-68	≥69	A
Handgrip strength <sup>67,68</sup>	≥32 kg ♂ ≥20 kg ♀	26-31.9 kg ♂ 16-19.9 kg ♀	19-25.9 kg ♂ 15.3-15.9 kg ♀	≤18.9 kg ♂ ≤15.2 kg ♀	A
Interview for Deterioration in Daily Living Activities in Dementia (IDDD) <sup>69</sup>	36 (initiation), 0 performance	36 (initiation), 0-2 performance	36 (initiation), 3-36 performance	36 (initiation), ≥37 performance	A
Katz ADL Index <sup>70</sup>	6	4-6	2-3	0-1	A
Knee extensor strength <sup>71</sup>	≥3.0 Nm/kg		<3.0 Nm/kg		A
Lawton IADL Index <sup>72</sup>	8	8	4-7	0-3	A
Minimum Data Set (MDS) ADL <sup>73,74</sup>	0	0-3	4-18	≥19	A
Modified Physical Performance Test (MPPT) <sup>75</sup>	32-36	19-31	3-18	≤2	A
Nürnberger Alters-Alltagsaktivitäten (NAA) Scale <sup>76</sup>	20	20-24	25-39	≥40	A
Nürnberger Alters-Beobachtungen (NAB) Scale <sup>76</sup>	15	15-19	20-29	≥30	A
Physical Self-Maintenance Scale (PSMS) ADL (range 0-6) <sup>72</sup>	6	3-6	1-2	0	A
Physical Self-Maintenance Scale (PSMS) original observer-rated version (range 6-30) <sup>77</sup>	6	6-10	11-21	≥22	A
Physical Self-Maintenance Scale (PSMS) self-rated version (range 8-24) <sup>78</sup>	24	21-24	10-20	≤9	A
6-Minute-Walk <sup>79</sup>	>300 m		≤300 m		A
Short Physical Performance Battery (SPPB) <sup>80</sup>	10-12	7-9	3-6	0-2	A
Timed Up and Go <sup>81</sup>	<10 s	≥10 and < 20 s	≥20 and < 30 s	≥30 s	A
Vulnerable Elders Survey (VES) 13 <sup>82,83</sup>	0 or 3 (if participant gets 3 points for age)	0-6 or 3-9 (if participant gets 3 points for age)	7-10 or 10 (if participant gets 3 points for age)		A
Alzheimer's Disease Cooperative Study (ADCS) ADL Scale <sup>84,85</sup>	78	72-78	38-71	≤37	A
Disability Assessment for Dementia (DAD) <sup>86,87</sup>	100%	>90%-100%	>47.5%-90%	≤47.5%	A
Epic Assessment System (EASY) Care <sup>88</sup>	49-50	51-59	60-80	≥81	A
Multidimensional Prognostic Index (MPI) <sup>89</sup>	0-0.33		0.34-0.66	0.67-1.0	A
Short Form (SF) 12 (PCS) <sup>90</sup>	50.5-56.6	40.3-50.4	29.7-40.2	≤29.6	A
Short Form (SF) 36 (PCS) <sup>91-93</sup>	48.7-64.0	29.6-48.6	21.2-29.5	≤21.1	A
Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie (SHERPA) <sup>94</sup>	0	0-1	1.5-3	3.5-11.5	A
Triage Risk Screening Tool (TRST) <sup>95</sup>	0	0-1	2-5		A
American Society of Anesthesiologists (ASA) Score <sup>96</sup>	I-II	II-III	III-IV	IV-V	B
Eastern Cooperative Oncology Group (ECOG) <sup>97</sup>	0		1-2	3-4	B
Falls Efficacy Scale-International (FES-I) <sup>98</sup>	16	17-32	33-48	49-64	B
Karnofsky Index <sup>99</sup>	100	80-90	60-70	10-50	B

(I)ADL, (instrumental) activities of daily living.

\*For the determination of cut-offs: see [supplement 2](#) and methods above.

heterogeneity of frailty definitions is huge. And because frailty has been defined primarily clinically, its etiology has been discussed in comparable complexity as its operationalization. Potential causative pathways that have been hypothesized include sarcopenia,<sup>31</sup> senescent immune remodeling,<sup>32</sup> neurodegeneration,<sup>33</sup> or even polypharmacy.<sup>34</sup> Therefore, frailty assessments sometimes even include biomarkers<sup>35</sup> or psychological parameters such as cognition (Edmonton Frail Scale<sup>36</sup>). This heterogeneity has led to the definition of derived concepts such as cognitive frailty,<sup>37</sup> cardiovascular frailty,<sup>38</sup> or social frailty.<sup>39</sup> The most common assessment instruments are the clinical phenotype model by Fried (the Frailty phenotype, often also called physical frailty)<sup>17</sup> and the deficit model by Rockwood and Mitnitski (the Frailty Index).<sup>40,41</sup> Although the frailty phenotype model includes mainly functional status items, the estimated frailty index according to the deficit model depends very much on the parameters collected in each study. As a result, it hardly ever includes the

same parameters and, for example, as demonstrated above, in the SPRINT study mostly assesses multimorbidity. Thus, in every study where deficit models are used to characterize frail older people, these models have to be judged individually according to our proposed criteria.

Following strictly our concept of functional impairment, we excluded those frailty scores that did not contain at least 25% physical functionality. Furthermore, not all models span the full range from no or little impairment to disability and dependency. Even physical frailty models such as the clinical phenotype by Fried usually do not include dependency, with the consequence of limited applicability to identify these functional states. Because treatment recommendations for many chronic diseases might not be different for frail older adults until evident disability occurs, as shown above, we need to span a wider range of functional status including dependency. Nevertheless, in the context of early identification of (imminent) frailty and prevention of

functional decline, frailty assessments and their implementation and application are still essential.

When rating evidence according to functional levels, several outcomes should be considered. An individual's personal preferences can change along the life course and, apart from overall survival, can range from longevity to quality of life or disability-free life years.<sup>42</sup> Terms such as quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs) have to be mentioned in this context as appropriate endpoints. As an example, frequent falls because of hypotension might be more threatening to an individual person than the risk of suffering a cerebral ischemia within the next years. However, cerebral ischemia can have catastrophic consequences, and physicians are responsible for clearing up any misunderstandings about the disabling results of a major stroke before they accept to withhold essential treatment. Guidelines including stratification of treatment goals according to physical frailty or functionality could support these clinical decisions. If no evidence for the functionally severely impaired is available, treatment choices should be made according to the available disease-specific guidelines. These considerations very clearly demonstrate the need to be as precise as possible when critically appraising evidence for individual diseases in older adults, and that tailoring treatment approaches according to chronological age never really hits the mark.

### Strengths and Limitations

Because of the non-systematic approach of our review, Tables 1 and 2 summarize only the most common instruments used in clinical settings and do not represent an exhaustive list. Nevertheless, our study proposes a new approach to disentangle functionality levels across different instruments and new instruments can always be added, following our approach. The decision that an assessment or score sufficiently reflects physical function is always contestable. We are aware that several proposed assessments do not primarily measure functional status and should be interpreted with caution and within the individual context. For certain indices the cut-off values were very difficult to determine and consensus not easy to reach. Especially, disentangling the functional levels “independent” and “slightly impaired” was not always possible or sometimes only resulted in very small differences. For example, when evaluating the Lawton IADL, we determined a difference of only 1 point between a functionally independent and a functionally significantly impaired patient, taking into account that only 1 of the inquired instrumental activities of daily living would most likely not be achievable for a significantly impaired older person, which is “taking care of all shopping needs independently.”

Tables 1 and 2 also include some assessments that do not explicitly measure functionality but provide information about general health such as the ASA Score and Karnofsky Index. In addition, from a conceptual point of view, a proxy-rated activities of daily living index cannot be compared with performance-based assessments such as gait speed or handgrip strength. However, this proposal has to be considered a reasoned viewpoint to provoke and inform further discussion about necessary changes in clinical trial planning for older people. In addition, because of the frequent lack of measurements on functionality, these instruments could still help to retrospectively characterize the study population in relation to the participants' functional limitation and/or dependency better than by simply using age as the primary stratifying variable. We encourage identifying more suitable assessments and adding them to our list by evaluation according to our proposed method. We are aware that cognitive impairment and mental health (eg, depression) are not explicitly included by focusing on functional status. However, as mentioned above, deficits in these domains also may lead to functional decline and disability downstream within the disablement process. Our strong focus on physical function allows for rating and

characterization of all kinds of different treatments from antihypertensives to antidementive or antidepressant therapies.

### Conclusion

According to the available evidence, differences in treatment effects and outcomes seem to affect mostly individuals with (severe) functional impairments and disability. Most clinical trials and observational studies in older adults have not included appropriate assessments to allow for a functional categorization of their participants. However, they might provide some other information about functional status, which could be used as a proxy to rate the population under study. For the retrospective characterization of frail and functionally impaired older people in clinical trials and observational studies, we propose cut-off points for 51 existing assessments on functional status and physical frailty across 4 common categories. The scientific and clinical community should strive for inclusion of appropriate assessments on functionality in every future study in order to clearly identify any of the following categories: independent, slightly impaired, significantly impaired, and disabled. Expanding the CONSORT reporting guideline with this item would further help to support the search, analysis, synthesis, and interpretation of evidence in older people not just based on the chronological age but according to one of the most critical modulators of clinical endpoints in older people: functional status.

### Supplementary Data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jamda.2018.11.008>.

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